

N'Guyen.

Applicants respectfully challenge the Examiner's conclusions in the final rejection on the ground that they are contrary to numerous established precedents in the field of chemical patent law, and also contrary to textbook chemistry. Applicants respectfully submit the following authorities and textbook for the Examiner's consideration.

First, it appears that the Examiner in the final rejection has selected portions of the N'Guyen reference upon which to base the final rejection, without a consideration of this reference as a whole. That is, the Examiner has relied on the disclosure of N'Guyen that a thiol (glutathione) is used in the chemical composition without considering the disclosure of N'Guyen that the thiol is coupled to a complexing agent.

The Court of Customs and Patent Appeals has long held in connection with rejections under 35 U.S.C. § 103, that it was improper to pick and choose from the relevant prior art only as much as will support a holding of obviousness, to the exclusion of other parts of a reference, which are necessary to fully appreciate what the prior art suggests to one skilled in the art. In re Wesslau, 353 F2d 238, 147 USPQ 391 (CCPA, 1965).

It is respectfully submitted that this same principle applies to references whether they are used in a rejection under 35 U.S.C. § 103 or 35 U.S.C. § 102. In this connection, it is respectfully submitted that the court has mandated that the Examiner must

consider all parts of the reference as a whole, and not merely a part of a reference will support the rejection.

In this connection, it is respectfully submitted that the N'Guyen reference when considered as a whole discloses that the antioxidant system based on a stabilized ascorbyl ester can be stabilized by a "complexing agent-thiol couple". See, for example, column 2, lines 45-53 and column 8, lines 24-30. (Examples of statements made by the patentee N'Guyen were cited on page 4 of the amendment filed on February 13, 2001). Therefore, it is respectfully submitted that the Examiner, in construing the N'Guyen reference, should consider all parts of this reference including the parts which teach that the thiol is coupled to the EDTA complexing agent. In view of the above authorities, ignoring this part of the N'Guyen reference which does not support the rejection is contrary to the above cited authorities. It therefore follows that the rejection fails as a matter of law.

Second, the Examiner in the final rejection states that the term "complexing agent-thiol couple" does not necessarily mean that the two agents have reacted or become chemically bound in any way.

Applicants are submitting herewith a number of pages from an Organic Chemistry textbook of Fessenden & Fessenden, Third Edition, copyright 1986, including the cover page, the page showing the copyright and publisher, the Library of Congress cataloging, pages 228, 240 and 498. It is respectfully submitted that this textbook shows that in coupling reactions between two chemical components,

the components are in fact reacted. See, for example, the reaction set forth in paragraph C on page 228 of the Organic Chemistry textbook, the top two reactions set forth on the top of page 240, and the description of coupling reactions set forth beginning in the middle of the page of page 498.

Applicants respectfully submit that the Organic Chemistry textbook shows that compounds that have been coupled simply means that they have been reacted with another compound. It is therefore respectfully submitted that in view of the textbook, "Organic Chemistry", Third Edition, it is clear that the coupling reaction in the N'Guyen reference refers to a reaction between the complexing agent and thiol.

Applicants also challenge the Examiner's attempt to shift the burden of proof to the applicants to prove by direct evidence that chemical coupling between the thiol and complexing agent occur as disclosed in the N'Guyen reference. If we are to follow the Examiner's suggestion that the burden lies with the applicants to prove that the complexing agent and thiol react, then we must disregard the statements of the patentee that the complexing agent and thiol are coupled. This raises the issue of whether a reference relied upon by the Examiner must be taken at face value and considered to be operable.

The authorities have long held that the disclosure of a reference must be taken at face value in the absence of evidence or reasoning inconsistent therewith. In re Donohue, 632 F2d 123, 207

USPQ 196 (CCPA, 1980) and Ex parte Naugokas, 17 USPQ 2d, 1587 (BPAI, 1989). Further, the Board has long held that the Examiner is required to demonstrate the inoperability of a U.S. patent. Ex parte Levy, 17 USPQ 2d 1461, 1463 (BPAI, 1990). In addition, it is well established that references are presumed to be operable. See Freeman v. Minnesota Mining and Manufacturing Co., 693 FedSup 134, 9 USPQ 2d 1111 (D.C. Del, 1998).

At the present time, the Examiner has failed to submit any evidence to demonstrate that the N'Guyen reference is inoperable or that the reactions disclosed therein, i.e., the specific reactions between the complexing agent and thiol, do not occur.

Consequently, it would constitute an error of law to conclude that it is applicants who have the burden of proving the reactions disclosed in the N'Guyen reference occur, i.e., that there is a reaction between the complexing agent and thiol.

Applicants also respectfully challenge the Examiner's statements in the argument bridging pages 5 and 6 of the final Office Action that if the "interactions proposed by applicants took place, it would defeat the purpose of the antioxidant compositions disclosed by the reference" and that this reference "must be considered to teach the use of glutathione in a chemically unreacted form". It is clear that the reference teaches that the complexing agent and thiol are coupled, i.e., reacted together. For the Examiner to conclude that the complexing agent-thiol couple would defeat the purpose of the antioxidant composition is

tantamount to the Examiner concluding that the reference is invalid.

It thus appears that the Examiner is challenging the validity of the N'Guyen reference if the reference as a whole is construed as requiring the use of the complexing agent-thiol coupled composition. However, the Examiner has provided no evidence whatever in support of his position that the complexing agent and thiol are not coupled.

Even assuming arguendo that the glutathione was present, for example, in the solar creams set forth in Table VI in unreacted form, it is respectfully submitted that one skilled in the art would conclude that the thiol (glutathione) reacts with the complexing agent (EDTA) since the reference as a whole teaches that these compounds are coupled. Therefore, in such a case, the glutathione would be present at most only in a transitory or intermediate condition.

However, it is well established that a product is not anticipated by a temporary, transitory and intermediate condition of a material of a prior art process. Instant Milk Co. v. Watson, Commr. Pats., 118 USPQ 50 (DCDC, 1957). See also In re LeGrice, 301 F2d 929, 133 USPQ 365, 374, 378 (CCPA, 1962). Therefore, it is respectfully submitted that any temporary or transitory presence of glutathione in the solar cream would not anticipate the method of use claims now set forth in the present application.

In view of the foregoing, it is respectfully submitted that

the final rejection fails as a matter of law in view of the various authorities discussed above. Consequently, the Examiner would be justified in no longer maintaining the rejection. Withdrawal of the rejection is accordingly respectfully submitted.

In view of the foregoing, it is respectfully submitted that this application is now in condition for allowance, and early action and allowance thereof is accordingly respectfully requested. In the event that there is any reason why the application cannot be allowed at the present time, it is respectfully requested that the Examiner contact the undersigned at the number listed below to resolve any problems.

Respectfully submitted

TOWNSEND & BANTA



Donald E. Townsend
Reg. No. 22,069

TOWNSEND & BANTA
1225 Eye Street, N.W.
Suite 500
Washington, D.C. 20005
(202) 682-4727

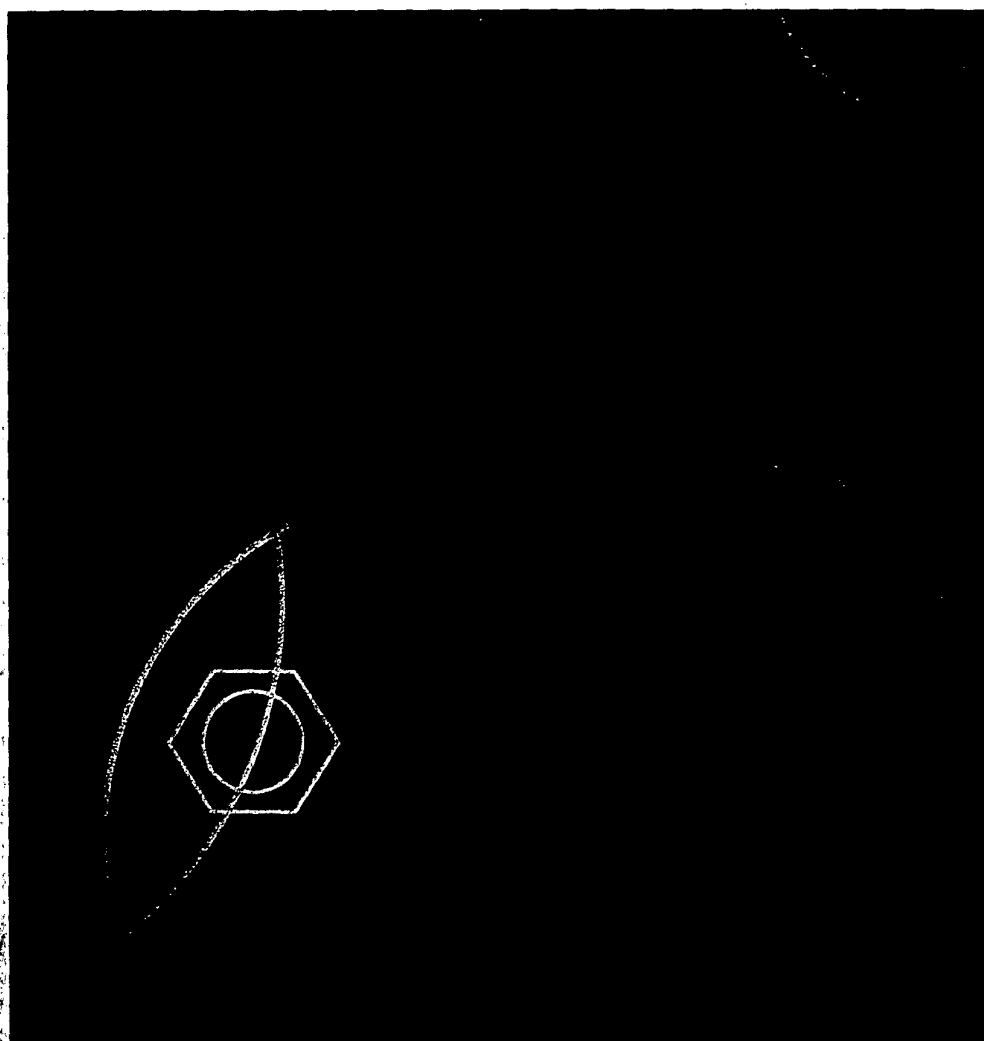
Date: June 25, 2001



FESSENDEN & FESSENDEN

Organic Chemistry

THIRD EDITION





Brooks/Cole Publishing Company
A Division of Wadsworth, Inc.

© 1986 by Wadsworth, Inc., Belmont, California 94002. Copyright © 1982 by PWS Publishers. Copyright © 1979 by Willard Grant Press. All rights reserved. No part of this book may be reproduced, stored in a retrieval system, or transcribed, in any form or by any means—electronic, mechanical, photocopying, recording, or otherwise—without the prior written permission of the publisher, Brooks/Cole Publishing Company, Monterey, California 93940, a division of Wadsworth, Inc.

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

Permission for the publication herein of Sadtler Standard Spectra® has been granted, and all rights are reserved, by Sadtler Research Laboratories, Division of Bio-Rad Laboratories, Inc.

Library of Congress Cataloging in Publication Data

Fessenden, Ralph J.

Organic chemistry.

Includes index.

1. Chemistry, Organic. I. Fessenden, Joan S.

II. Title.

QD251.2.F49 1982 547 81-13496

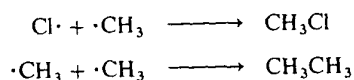
ISBN 0-534-05088-3

Sponsoring Editor: Sue Ewing
Project Development Editor: David Chelton
Editorial Assistant: Lorraine McCloud
Production: Unicorn Production Services, Inc.
Cover Design: Jamie Sue Brooks
Cover Illustration: Pauline Phung
Typesetting: Composition House, Ltd.
Printing and Binding: R. R. Donnelley & Sons Co., Willard, Ohio

C. Termination

The propagation cycle is broken by **termination reactions**. Any reaction that results in the destruction of free radicals or in the formation of stable, nonreactive free radicals can terminate the free-radical propagation cycle. The chlorination of methane is terminated principally by free radicals combining with other free radicals; this is a process of destruction of free radicals. In Section 6.7, we will mention termination by formation of stable, nonreactive free radicals.

Termination steps:



The second termination step shown is an example of a **coupling reaction**: the joining together of two alkyl groups.

STUDY PROBLEM

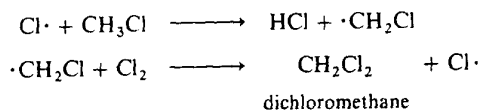
- 6.2 Write equations for the initiation, propagation, and termination reactions leading to the formation of chlorocyclohexane from cyclohexane and chlorine.

D. Why free-radical reactions yield mixtures of products

Free-radical reactions are often characterized by a multitude of products. For example, the chlorination of methane can yield four organic products. The reason for the formation of these mixtures is that the high-energy chlorine free radical is not particularly selective about which hydrogen it abstracts during the propagation step.

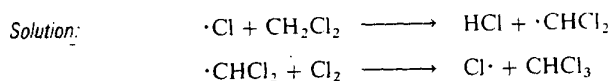
While chlorine is undergoing reaction with methane, chloromethane is being formed. In time, the chlorine free radicals are more likely to collide with chloromethane molecules than with methane molecules, and a new propagation cycle is started. In this new cycle, chloromethyl free radicals ($\cdot\text{CH}_2\text{Cl}$) are formed. These undergo reaction with chlorine molecules to yield dichloromethane (CH_2Cl_2). As in the previous cycle leading to CH_3Cl , another chlorine free radical is regenerated in the process.

Propagation steps leading to dichloromethane:



SAMPLE PROBLEM

Write the propagation steps leading to the formation of trichloromethane (chloroform) from dichloromethane.



STU

6.3 Writ
(car)mon
nun
into

STU

6.4 How

SAMPLE

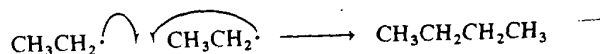
A c
to a
of CSol
pro
of c

SECTION 6

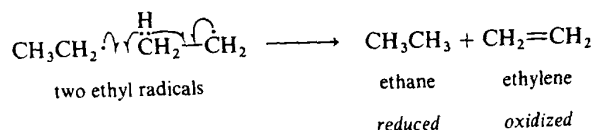
Re

The
rad
Chl
towwith
ene
alm

Termination by coupling (joining together):



Termination by disproportionation (oxidation-reduction of two equivalent species):



Controlled pyrolysis has been used industrially for the cracking of high-molecular-weight compounds into lower-molecular-weight compounds. Until about 1925, pyrolysis of wood was the major source of methanol (wood alcohol). Thermal cracking was once the only petroleum cracking technique available. Now, the cracking of petroleum is accomplished with catalysts (Section 3.5), while methanol is largely produced by the catalytic hydrogenation of carbon monoxide ($\text{CO} + 2\text{H}_2 \rightarrow \text{CH}_3\text{OH}$).

B. Oxygen as a free-radical reagent

Molecular oxygen is different from the compounds we have been studying so far because a stable molecule of O_2 in the ground state has two unpaired electrons; oxygen is said to be a **diradical**. The structure of O_2 cannot be adequately explained by valence-bond formulas because one pair of $2s$ electrons is in an antibonding orbital. For our purposes, we will represent molecular oxygen as $\cdot\text{O}-\text{O}\cdot$ or simply O_2 .

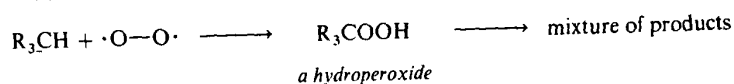
Oxygen is a stable diradical and therefore is a selective free-radical agent. A compound that contains double bonds, allylic or benzylic hydrogens, or tertiary hydrogens is susceptible to **air oxidation**, also called **auto-oxidation** or **autoxidation**. Compounds with only primary and secondary hydrogens are not as susceptible. (From our discussion of free-radical halogenation reactions, the relative reactivities of these hydrogens should not be surprising.)

Fats and vegetable oils often contain double bonds. Auto-oxidation of a fat yields a mixture of products that includes low-molecular-weight (and foul-smelling) carboxylic acids. For example, rancid butter contains the odorous butanoic acid.

Linseed oil and other vegetable oils, which contain many double bonds, are used as drying oils in paint and varnish. These compounds are purposely allowed to undergo air oxidation because the molecules join together, or *polymerize*, into a tough film on the painted surface.

Auto-oxidation initially leads to **hydroperoxides**, compounds containing the $-\text{OOH}$ group, which are readily converted to mixtures of alcohols, ketones, and other products. Because mixtures are the usual result, auto-oxidation is rarely used as an organic synthetic technique.

Auto-oxidation:



prod
adjac
heate
by di
reduc
as th

by re

STUD

6.10 When
than c

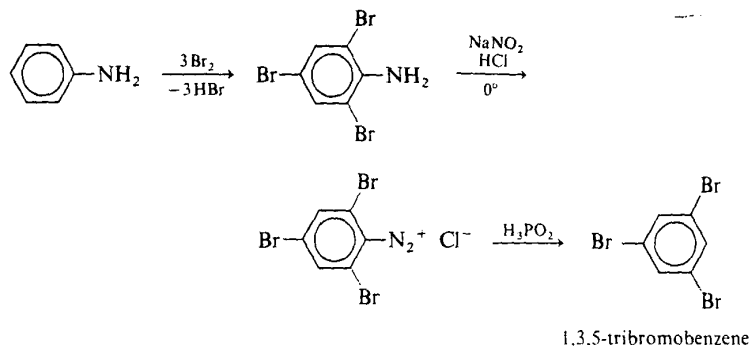
SECTION 6.7

Free

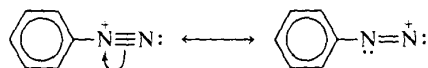
A fre
action
There
to ini
called
consu

initiat
becau

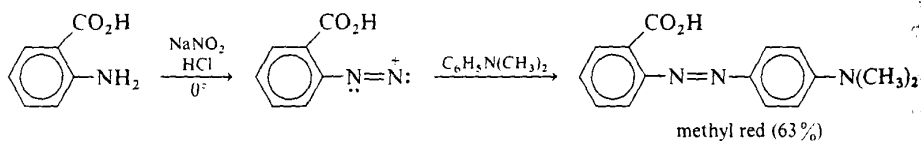
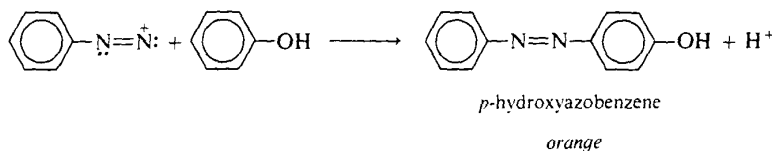
Solution: Recall from page 485 that aniline undergoes tribromination readily. Therefore, the following reaction sequence will yield the desired product:



Coupling reactions. Coupling reactions of aryldiazonium salts are used to prepare dyes from aniline and from substituted anilines. In these reactions, the diazonium ion acts as an *electrophile*. Resonance structures for the diazonium ion show that both nitrogens carry a partial positive charge.



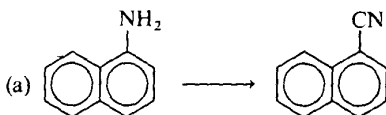
The terminal nitrogen attacks the *para*-position of an activated benzene ring (one substituted with an electron-releasing group like NH_2 or OH). The coupling product contains an **azo group** ($-\text{N}=\text{N}-$) and is generally referred to as an **azo compound**. Many azo compounds are used as dyes (see Section 21.5B).



The reactions of aryldiazonium salts are summarized in Figure 10.12.

STUDY PROBLEM

- 10.17 How would you make the following conversions? In (c), use no aromatic reagent other than benzene.



(b) CH

(c)  $\text{ArN}_2^+ \text{Cl}^-$

FIGURE

SECTION 10.15

Halob

In Cha
and eli
strengtUnder
aromatiAlthoug
differen
 E^+ , not